REMARKS

Claims 1, 4-13, and 16-18 are pending in the subject application. Claims 1, 5-10, 13 and 17 are amended herein. In particular, claim 1 has been amended to recite that R^8 may represents a group of the formula -O-C(O)-R^{16}, -O-C(O)-$NR^{17}R^{18}$, -C(O)-OR^{19}, -NR^{20}-C(O)-R^{21} or -NR^{22}-C(O)-$NR^{23}R^{24}$. Support for this amendment can be found in paragraphs 110, 117, 121, 124 and 128 of the published patent application and in the claims as originally filed. Similarly, Claims 1 and 6 have been amended to recite that R^{16} may represent (C_1-C_8)-alkyl substituted by phenyl, cyclopentyl, cyclohexyl, (C_1-C_4)-alkoxy or up to three times by fluorine. Support for this amendment can be found in paragraph 143 of the published patent application. Other amendments to claims 1, 5-10, 13 and 17 are made solely to more clearly define the claimed subject matter. No new matter has been added by the amendments. Support for the amendments and new claims is found throughout the application as originally-filed and from the pending and original claims

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited by the Examiner, and that these claims were in full compliance with the requirements of 35 U.S.C. § 112. The amendment of the claims, as presented herein, is not made for purposes of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112. Rather, this amendment is made simply for clarification and to round out the scope of protection to which Applicants are entitled. Furthermore, it is explicitly stated that the amendments made herein should not give rise to any estoppel.

Reconsideration and withdrawal of the objections to and the rejections of this application in view of the amendments and remarks herewith, is respectfully requested, as the application is believed to be in condition for allowance.

Applicants respectfully reserve the right to pursue any non-elected, canceled or otherwise unclaimed subject matter in one or more continuation, continuation-in-part, or divisional applications.

Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1, 4-13, and 16-18 stand rejected as being indefinite as the formulas which are represented by R^2 are allegedly ambiguous with respect to the point of attachment.

Without conceding the validity of the Examiner's rejections, claim 1 has been amended to clarify the point of attachment for the formulas represented by R^2. This point of attachment is signified in the amended structures as a wavy line across the point of attachment. No new matter has been added by this amendment. Support for these amendments can be found throughout the application and claims as originally filed. Applicants respectfully request reconsideration and withdrawal of these rejections.

Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1, 4-5, 13 and 16-18 stand rejected as failing to provide written description for the claims in that no nexus is shown between the inhibition of cholesterol ester transfer protein ("CETP") and "any and all known or unknown diseases". Applicants respectfully disagree.

Claims 1, 4-5, 13 and 16-18 are directed to methods of treating a disorder controlled by inhibition of CETP. The claims are not directed, as the Examiner suggests, to the treatment of any and all known or unknown diseases but only to those diseases which are associated with the overproduction of CETP. Indeed, one of skill in the art would readily recognize which diseases are so associated and thus which would be treatable by the methods encompassed by the present claims. Furthermore, the specification states, by way of example, that "the compounds according to the invention are highly active inhibitors of the cholesterol ester transfer protein (CETP) and stimulate reverse cholesterol transport...[and] can therefore be employed for the treatment and prevention of hypolipoproteinaemia, dyslipidaemias, hyper-triglyceridaemias, hyperlipidaemias or arteriosclerosis.... adiposity and obesity....stroke and of Alzheimer's disease."

As such, Applicants respectfully assert that the claims as originally presented and as herein amended, are in full compliance with the requirements of 35 U.S.C. § 112. Reconsideration and withdrawal of the rejections is respectfully requested.

Claims 1, 4-5, 13 and 16-18 stand further rejected as failing to provide enablement for preventing diseases. Although Applicants strongly disagree with the Examiner's allegation that the specification is viewed as lacking enablement for prevention of any of the diseases recited, the pending claims have been amended to delete the terms "or preventing," solely to expedite the prosecution of the present application, and without prejudice to Applicants' right to pursue them in one or more continuation, divisional or continuation-in-part applications. In view of these

amendments and the following discussions, Applicants respectfully submit that the rejection must be withdrawn.

Finally, claims 1, 4-5, 13, and 16-18 stand rejected as allegedly failing to enable "the instant compound to alter the gene expression and therefore to treat any and all known or unknown diseases." Applicants respectfully traverse.

With regard to the methods of treatment defined by the present claims, the test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. U.S. v. Telectronics, Inc., 857 F.2d 778, 785 (Fed. Cir. 1988). The examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. Manual of Patent Examining Procedure ("MPEP") § 2164.04 (citing In re Wright, 999 F.2d 1557, 1562 (Fed. Cir. 1993)).

Accordingly:

> A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must be taken as being in compliance with the enablement requirement ... unless there is a reason to doubt the objective truth of the statements contained therein* which must be relied on for enabling support
>
> * * *
>
> It is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.
> *Id. (emphases added).*

Applicants respectfully submit that whether or not the scope of a claim is broad is irrelevant to the assessment of the enablement of the claim. The question is whether those skilled in the art would have been able to make and use the claimed invention based on the disclosure. (See *U.S. v. Telectronics, Inc., at 785*).

Applicants respectfully submit that the pending claims are enabled because the specification "contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented." *Id.*

As stated above, the specification states, by way of example, that "the compounds according to the invention are highly active inhibitors of the cholesterol ester transfer protein (CETP) and stimulate reverse cholesterol transport...[and] can therefore be employed for the treatment and prevention of hypolipoproteinaemia, dyslipidaemias, hyper-triglyceridaemias, hyperlipidaemias or arteriosclerosis.... adiposity and obesity....stroke and of Alzheimer's disease." The specification further states "The active compounds according to the invention cause a lowering of the LDL cholesterol level (low density lipoprotein) in the blood together with a simultaneous increase in the HDL cholesterol level (high density lipoprotein)."

Similarly, it is disclosed that the claimed compounds can be prepared by synthetic procedures described in Examples 1-151. Therefore, it is clear that sufficient guidance is provided in the specification to allow those of ordinary skill in the art to make and use the claimed invention, as required by 35 U.S.C. § 112, first paragraph.

Nonetheless, the Examiner further alleges that one skilled in the art would have to engage in an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims. Applicants respectfully disagree with these allegations.

In view of the foregoing, it is clear that sufficient guidance is provided in the specification so as to allow those of ordinary skill in the art to make and use the claimed invention. Indeed, the claimed invention is directed to the use of obtainable compounds. The determination by a physician as to whether a claimed compound is effective in treating a recited disease in a given patient is a type of determination that is always made by physicians for every pharmaceutical. Indeed, the determination is a routine one that every physician is prepared to make, and which requires little or no effort. Therefore, Applicants respectfully submit that one reasonably skilled in the art could make or use the invention as claimed without undue experimentation.

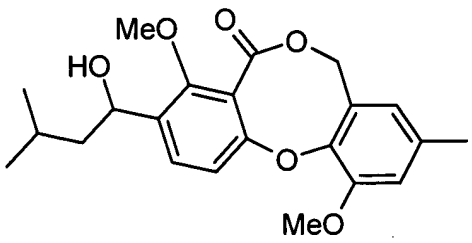
Therefore, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn

Rejections under 35 U.S.C. § 102

A. Pettibone

Claims 1, 4-5 and 18 stand rejected under 35 USC §102(b) as being anticipated by U.S. Patent No. 5,198,463 to Pettibone et al. ("Pettibone"). Pettibone teaches methods of inhibiting oxycontin activity by administration of a penicillide compound.

Applicants respectfully traverse the rejection. Pettibone does not encompass all the teachings of amended claims 1, 4-5 and 18 of the instant invention. In particular, the Examiner alleges that Pettibone discloses a compound having the formula:



While it may be true that the genus disclosed by Pettibone encompasses such a compound, Pettibone neither teaches this compound specifically nor how to make or use such a compound. Indeed, the specific compound relied upon by the examiner is specifically excluded by Pettibone in the claims. Nevertheless, claim 1 has been amended to recite that R^8 may represents a group of the formula -O-C(O)-R^{16}, -O-C(O)-$NR^{17}R^{18}$, -C(O)-OR^{19}, -NR^{20}-C(O)-R^{21} or -NR^{22}-C(O)-$NR^{23}R^{24}$. As such, Pettibone does not teach or disclose any specific compounds encompassed by the amended claims.

With regard to claims 1, 4-5 and 18, it is respectfully noted that Pettibone does not teach or disclose the use of any of its compounds (or compositions comprising those compounds) in a methof for treating a disorder controlled by the inhibition of cholesterol ester transfer protein.

As Pettibone does not anticipate the instant invention, Applicants respectfully request reconsideration and withdrawal of the rejection.

B. Nishida

Claims 1, 4-6 and 11-18 stand rejected under 35 USC §102(b) as being anticipated by Nishida *et al., Journal of Antibiotics,* 1991, 44, 152-9 ("Nishida"). Nishida teaches acylated derivatives of penicillide useful as acyl-CoA:cholesterol acyltransferace inhibitors.

Applicants respectfully traverse the rejection. Pettibone does not encompass all the teachings of amended claims 1, 4-6 and 11-18 of the instant invention. The Examiner alleges that compounds 4, and 9-12 of Nishida are encompassed by the present invention. As an initial matter, Applicants respectfully point out that compounds 4, 9, 10 and 12 of Nishida were not encompassed by the claims as originally filed. In particular, R^8 does not encompass Tetrahydro-pyranoxy (compound 4); R^{12} does not encompass a propyl or pentadecyl ester (compound 10 and 12) and R^{16} does not encompass pentadecane (compound 9). With respect to compound 11 and as discussed above, Claims 1 and 6 have been amended to recite that R^{16} may represent $(C_1\text{-}C_8)$-alkyl substituted by phenyl, cyclopentyl, cyclohexyl, $(C_1\text{-}C_4)$-alkoxy or up to three times by fluorine. Compound 11 of the reference bears an unsubstituted propyl substituent. As such, Nishida does not teach or disclose any specific compounds encompassed by the amended claims.

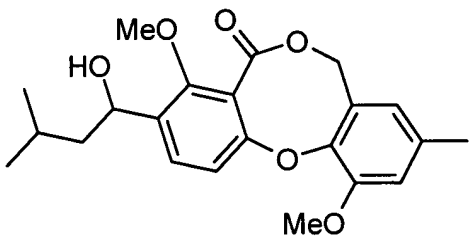
Finally, Applicants are unable to determine how Nishida relates to the compounds of claims 11 or 12 as originally presented as none of the compounds of Nishida are encompassed by the definition of R^8 in any of these claims. Applicants respectfully request withdrawl and/or clarification of this rejection.

As Nishida does not anticipate the instant invention, Applicants respectfully request reconsideration and withdrawal of the rejection.

C. Suzuki

Claims 1, 4-5 and 18 stand rejected under 35 USC §102(b) as being anticipated by U.S. Suzuki *et al. Phytochemistry,* 1991, Vol. 30, 2096-2098. ("Suzuki"). Suzuki teaches penicillide and dehydroisopenicillide isolated from *Talaromyces derxii* cultivated on rice.

Applicants respectfully traverse the rejection. Suzuki does not encompass all the teachings of amended claims 1, 4-5 and 18 of the instant invention. The Examiner alleges that Suzuki discloses a compound having the formula:



As discussed above, claim 1 has been amended to recite that R^8 may represents a group of the formula -O-C(O)-R^{16}, -O-C(O)-$NR^{17}R^{18}$, -C(O)-OR^{19}, -NR^{20}-C(O)-R^{21} or -NR^{22}-C(O)-$NR^{23}R^{24}$. As such, the instant claims do not encompass the compound described above nor does Suzuki teach or disclose any specific compounds encompassed by the amended claims. Furthermore, with regard to claims 1, 4-5 and 18, it is respectfully noted that Suzuki does not teach or disclose the use of any of its compounds (or compositions comprising those compounds) in a method for treating a disorder controlled by the inhibition of cholesterol ester transfer protein. Indeed, Suzuki is limited only to the isolation and identification of compounds.

As Suzuki does not anticipate the instant invention, Applicants respectfully request reconsideration and withdrawal of the rejection.

D. Frobel

Claims 1, 4-5 and 18 stand rejected under 35 USC §102(b) as being anticipated by U.S. Patent No. 5,089,487 to Frobel et al. ("Frobel"). Frobel teaches cardioactive compounds and methods of controlling the performance of the heart using the compounds taught therein.

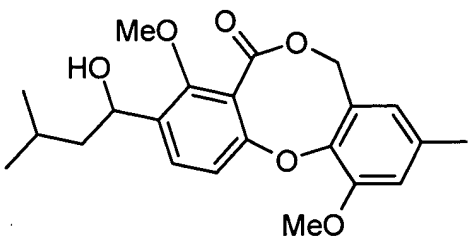
Applicants respectfully traverse the rejection. As an initial matter, Applicants respectfully point out that a number of the examples highlighted by the Examiner were not encompassed by claim 1 as originally filed (*See, e.g.*, Examples 10-13, 17, 24, 26-28, 32-34, 42, 48-49, 60-63, *et al.*). As discussed above, claim 1 has been amended to recite that R^8 may represents a group of the formula -O-C(O)-R^{16}, -O-C(O)-$NR^{17}R^{18}$, -C(O)-OR^{19}, -NR^{20}-C(O)-R^{21} or -NR^{22}-C(O)-$NR^{23}R^{24}$. As such, the instant claims do not encompass the compounds highlighted by the Examiner. Furthermore, none of the compounds disclosed by Frobel are encompassed by the amended claims.

As Frobel does not anticipate the instant invention, Applicants respectfully request reconsideration and withdrawal of the rejection.

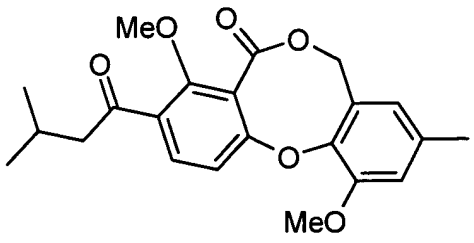
E. Sassa

Claims 1, 4-5 and 18 stand rejected under 35 USC §102(b) as being anticipated by Sassa *et al., Tetrahedorn Letters*,1974, Vol. 45, 3941-2. ("Sassa"). Sassa teaches a highly methylated fatty acid isolated from mycelial extracts of a *Penicillium sp.* Fungus.

Applicants respectfully traverse the rejection. Sassa does not encompass all the teachings of amended claims 1, 4-5 and 18 of the instant invention. The Examiner alleges that Sassa discloses a compound having the formula:



or



The Examiner has relied upon the results of an STN search in determining the disclosure of these compounds. Applicants agree that Sassa discloses the first compound cited by the Examiner but are unable to locate any reference to the second compound cited by the Examiner. Indeed, the Examiner has not shown where in Sassa the second compound is disclosed. Applicants respectfully request clarification of this rejection.

Nevertheless, and as discussed above, claim 1 has been amended to recite that R^8 may represent a group of the formula -O-C(O)-R^{16}, -O-C(O)-$NR^{17}R^{18}$, -C(O)-OR^{19}, -NR^{20}-C(O)-R^{21} or -NR^{22}-C(O)-$NR^{23}R^{24}$. The instant claims do not encompass either of the compounds described above. Therefore, Sassa does not teach or disclose any specific compounds encompassed by the amended claims. . Furthermore, with regard to claims 1, 4-5 and 18, it is respectfully noted that Sassa does not teach or disclose the use of any of its compounds (or compositions comprising those compounds) in a method for treating a disorder controlled by the inhibition of cholesterol ester transfer protein. Indeed, Sassa is limited only to the synthesis and identification of compounds.

As Sassa does not anticipate the instant invention, Applicants respectfully request reconsideration and withdrawal of the rejection.

CONCLUSION

In view of the amendments and remarks made herein, the application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are respectfully requested. Please charge any required fee or credit any overpayment to Deposit Account No. 041105.

Respectfully submitted,

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